

REMARKS/ARGUMENTS

Claims 1, 4-7, and 9-28 are pending in the present application.

The following remarks are believed to be fully responsive to the Office Action.

THE REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

SHOULD BE WITHDRAWN

Claims 1, 4-7, and 9-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for any or all iodium salt and fluoridation any or all aromatic or heteroaromatic compounds generically embraced in claim 1 and compounds with diverse structure embraced in claims 15-18. The examiner applies a number of factors in consideration of enablement, citing *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman* 230 USPQ 546. Taking each of the Examiner's observations in turn, Applicants responses are as follows:

The Examiner reasons that instant claims recite fluoridation of any iodonium salt and that the fluoridation reaction can take place at either side of the iodonium ion. The Examiner additionally states that there is no guarantee that the reaction would occur to yield fluorinated aryl or heteroaryl. In response, claim 1 was limited to recite that the iodonium salt comprises aromatic groups on both sides of the iodonium ion. It is abundantly clear therefore that only an aromatic fluoridated product can result when the method of present claim 1 is carried out. This point was made in response to the previous office action (page 13 second paragraph of the Response dated October 30, 2008). In addition, it is also relevant to note that the starting iodonium salt as defined in present claim 1 is specifically tailored such that

the aromatic ring Q is more electron deficient than the other aromatic ring (substituted with R1-5), ensuring that fluoridation occurs on ring Q.

The Examiner goes on to submit that, as the starting iodonium salt is permitted to be any compound, reactive groups which may also participate in the fluoridation reaction are not excluded. Firstly, the present scope of the claims cannot be said to encompass any iodonium salt, as it has been limited to recite only those of Formula I or Formula II. Furthermore, the definition of these formulae is tailored such that fluoridation takes place on Q, the most electron-deficient ring (as discussed in the previous paragraph). Accordingly, it is not likely to be an issue with reactive groups participating in the fluoridation reaction. Secondly, and as submitted in our previous response, the skilled person would in any case appreciate where protecting groups would be required (page 11 lines 2-4 refer to the common general knowledge relating to protecting groups). A limiting amendment presents itself as well: the specification provides that P1-P4 as defined for the precursor compounds in Table 1 may be hydrogen or a protecting group (page 11 lines 1-2). The precursor compounds of Table 1 are those of claim 15 - therefore this definition for P1-P4 should be introduced into claim 15. Such an amended claim 15 clearly specifies how to address the issue of reactive groups that may interfere with the fluoridation reaction.

The Examiner states that there is no teaching in the specification of how fluoridation of the compounds of claim 1 is achieved, or what starting material is used. This comment appears to be specifically addressed to starting iodonium salts comprising reactive groups that may interfere with the fluoridation reaction. The comments of the previous paragraph herein

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apply here. Overcoming this objection may be speeded by the limitation of claim 1 to the

subject matter of claim 15, including definition of P1-P4 as each being hydrogen or a

protecting group (as discussed above).

The Examiner additionally objects that, as there is a degree of unpredictability in the prior art, it is likely that the claims encompass significant numbers of inoperative embodiments.

The invention resides in the fact that, going directly against the teachings of the prior art relating to radiodfluoridations, radiofluoridation of iodonium salts in the presence of water results in yields comparable with, and in many cases greater than, the yield obtained from known processes. The examples in the specification test the method of the invention for different iodonium salt starting compounds and demonstrate that, in the presence of water, the fluoridation reaction takes place as desired, or with an improved yield. Therefore, the stated benefits of the invention have been found to apply to divergent iodonium salt structures, and there is no reason why these stated benefits would not apply over the whole range of the claims.

The Examiner reiterates that there is no teaching to enable the method of the invention to be carried out where there are reactive groups in the starting iodonium salt that would interfere with the radiodfluoridation reaction. Again, the comments made above in relation to reactive groups and protecting groups are relevant here. That is, the person skilled in the art would know where a protecting group would be required, and if the subject matter of claim 15 along with definition for P1-P4 is included in claim 1, there is a clear indication that protecting groups may be required.

The Examiner also submits that the skilled person would have to undergo an undue amount of experimentation to use the claimed invention commensurate with the scope of the claims. The method of the invention is simply that taught in detail in the prior art but using a defined amount of water in the reaction solvent. The skilled person (who is skilled in the art of radiochemistry) would be familiar with the existing methods and would be able to adapt them without undue effort.

Therefore, Applicants respectfully request that the rejections of the 35 U.S.C. 112, first paragraph, of claim 1, 4-7, and 9-28 be withdrawn.

THE REJECTIONS UNDER 35 U.S.C. § 103
SHOULD BE WITHDRAWN

Claims 1, 4-7, and 18-28 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Grushin et al. (Grushin). In response, Applicants submit that each of the rejections should be withdrawn for the reasons stated below.

The method of the present invention is for the radiofluoridation of iodonium salts and the teaching of Grushin cited by the examiner clearly does not relate to the fluorination step. Furthermore, the common general knowledge in the art of radiochemistry is an essential step for carrying out radiofluoridation is the removal of water (please see attached pages 196-201 from Handbook of Radiopharmaceuticals by Welch and Redvanly, 2003 Wiley and in

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particular the first paragraph under the heading "Nucleophilic Fluorination" on page 197
outlining "crucial" steps, and the second paragraph on page 198). There is a strong teaching
in the common general knowledge that, in order for a successful reaction to take place, water
should not be present in the radiofluorination reaction and should be actively removed from
fluoride ion before it is used in the reaction. Therefore the method of the present claims goes
directly against this teaching, and the observations documented in examples 1-11 of the
specification are contrary to what the skilled person would expect to find.

Applicants respectfully submit that an unobvious step resides in the method and associated
kit of the present claims. The strategy is diametrically opposite the teachings of the common
general knowledge, the outcome as demonstrated in the (numerous) examples is unexpected,
and the benefit is that a step in the process can be omitted without compromising (and in
some cases even improving) the success of the synthesis. In a method of radiofluoridation
removal of a step means that the method is easier and takes less time, which means retaining
more of the radioactivity in the final product.

In view of the foregoing, it is respectfully submitted that 35 U.S.C. 103(a) rejections of
claims 1, 4-7, and 18-28 over Grushin be withdrawn.

CONCLUSION

In view of the amendments and remarks herein, Applicants believe that each ground for
rejection or objection made in the instant application has been successfully overcome or

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obviated, and that all the pending claims are in condition for allowance. Withdrawal of the
Examiner's rejections and objections, and allowance of the current application are
respectfully requested.

The Examiner is invited to telephone the undersigned in order to resolve any issues that
might arise and to promote the efficient examination of the current application.

Respectfully submitted,

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